

WHAT IS CLAIMED IS:

1. A method for the synthesis of peptides, peptide mimetics and/or proteins and/or for the selective N-terminal modification of peptides, peptide mimetics and/or proteins, with the steps of:
  - a) providing an amino component, said amino component having at least one amino acid,
  - b) providing a carboxyl component, said carboxyl component having a leaving group on the carboxyl group, and said carboxyl component being a compound having at least one amino acid or a compound having at least one label or reporter group,
  - c) reacting said amino component and said carboxyl component in a reaction medium which has one or more ionic liquids, in the presence of a protease, peptidase and/or hydrolase, to form a peptide bond between the amino component and the carboxyl component with elimination of the leaving group.
2. The method as claimed in claim 1, further comprising the step of:
  - d) enriching and/or isolating the resulting peptide, peptide mimetic and/or protein by methods known per se.
3. The method as claimed in claim 1 or 2, characterized in that the amino component is a polypeptide or protein.
4. The method as claimed in one or more of the preceding claims, characterized in that the amino component has a size of from 1 to 1000 amino acids, preferably from 30 to 500 amino acids, more preferably from 30 to 250 amino acids.
5. The method as claimed in one or more of the preceding claims, characterized in that the carboxyl end of the amino component is present protected or unprotected in nonactivated form.
6. The method as claimed in one or more of the preceding claims, characterized in that the N<sup>α</sup>-amino function of the amino component is present unprotected, and this

N<sup>α</sup>-amino function reacts with the carboxyl function of the carboxyl component.

7. The method as claimed in one or more of the preceding claims, characterized in that the carboxyl component is a polypeptide or protein.
8. The method as claimed in one or more of the preceding claims, characterized in that the carboxyl component has a size of from 1 to 1000 amino acids, preferably from 30 to 500 amino acids, more preferably from 30 to 250 amino acids.
9. The method as claimed in one or more of the preceding claims, characterized in that the carboxyl group of the carboxyl component forms a carboxylic ester or a carboxamide with the leaving group.
10. The method as claimed in one or more of the preceding claims, characterized in that the leaving group of the carboxyl component is selected from the group consisting of unsubstituted and substituted -O-alkyl-, -O-aryl-, -S-alkyl-, -S-aryl radicals, -NH-alkyl-, -NH-aryl-, -N,N-dialkyl-, -N,N-diaryl- and -N-aryl-N-alkyl- radicals.
11. The method as claimed in claim 10, characterized in that the leaving group of the carboxyl component is substituted by one or more carboxylic acid radicals, sulfonic acid radicals or sulfonates.
12. The method as claimed in one or more of the preceding claims, characterized in that the leaving group is a 4-guanidinophenyl, 4-amidinophenyl, 4-guanidinophenylthio or 4-amidinophenylthio radical, or a compound structurally homologous thereto.
13. The method as claimed in one or more of the preceding claims, characterized in that the leaving group is adjusted to the specificity of the protease, peptidase and/or

hydrolase used.

14. The method as claimed in one or more of the preceding claims, characterized in that the carboxyl component containing the leaving group has the following structure:



where Y = an N-terminal protecting group or is H,

Xaa = any  $\alpha$ -amino acid,  $\beta$ -amino acid or a derivative thereof, or is a label or reporter group,

R is a leaving group, in particular a leaving group which is selected from the group consisting of unsubstituted and substituted -O-alkyl, -O-aryl-, -S-alkyl-, -S-aryl- radicals, preferably 4-guanidinophenyl, 4-amidinophenyl, 4-guanidinophenylthio-, 4-amidinophenylthio radicals, each of which may be substituted by sulfonic acid groups or sulfonates, and also structural homologs thereof,

n is an integer of from 1 to 1000, preferably from 30 to 500, more preferably from 30 to 250.

15. The method as claimed in one or more of the preceding claims, characterized in that the carboxyl component is a label or reporter group selected from fluorescent labels containing carboxyl groups, such as fluorescein, rhodamine, tetramethylrhodamine, 2-aminobenzoic acid, isotopic labels containing carboxyl groups, such as  $^{13}\text{C}$ -,  $^{15}\text{N}$ - and  $^{17}\text{O}$ -containing amino acids or peptide fragments; spin labels containing carboxyl groups, such as nitroxide label-containing amino acid and fatty acid derivatives; biotin; crosslinking agents containing carboxyl groups, such as diazoacetate, diazopyruvate, p-nitrophenyl-3-diazopyruvate; 2-(1,2-dithiolan-3-yl)acetate; N,N'-1,2-phenylenedimaleimide; N,N'-1,4-phenylenedimaleimide.
16. The method as claimed in one or more of the preceding claims, characterized in that

the steps a) to c) and optionally d) are carried out twice or more, in order to prepare sequentially a polypeptide or protein which may have a label or reporter group.

17. The method as claimed in one or more of the preceding claims, characterized in that a compound prepared according to steps a) to c) and optionally d) is used as the amino component and another compound prepared according to steps a) to c) and optionally d) is used as the carboxyl component.
18. The method as claimed in one or more of the preceding claims, characterized in that the reaction medium has exclusively one or more ionic liquids.
19. The method as claimed in one or more of claims 1 to 17, characterized in that the reaction medium comprises one or more ionic liquids and also water, and/or an organic solvent and optionally customary additives.
20. The method as claimed in one or more of the preceding claims, characterized in that the proportion of ionic liquids in the reaction medium is 50 - 100% by volume, preferably 70 - 100 or 80 - 100% by volume, more preferably 90 - 100% by volume, likewise preferably from 95 to 100% by volume or 95 - 99% by volume.
21. The method as claimed in one or more of the preceding claims, characterized in that the cations of the ionic liquids used are quaternized alkylimidazolium ions, quaternized alkylammonium ions, quaternized alkylpyridinium ions and/or quaternized alkylphosphonium ions.
22. The method as claimed in claim 21, characterized in that the alkyl radicals of the ionic liquids are branched or unbranched and have 1 - 20 carbon atoms, preferably 2 - 10 carbon atoms, more preferably 4 - 6 carbon atoms.

23. The method as claimed in one or more of the preceding claims, characterized in that the ionic liquids used are 1-ethyl-3-methylimidazolium, 1-butyl-3-methylimidazolium and/or 4-methyl-N-butylpyridinium salts.
24. The method as claimed in one or more of the preceding claims, characterized in that the anions of the ionic liquids used are chloride, bromide, chloroaluminate, nitrate, benzenesulfonate, triflate (trifluoromethanesulfonate), tosylate and/or tetrafluoroborate.
25. The method as claimed in one or more of the preceding claims, characterized in that the protease used is a cysteine protease or serine protease.
26. The use of ionic liquids as an exclusive solvent or in combination with water and/or organic solvents for the synthesis and/or N-terminal modification of peptides, peptide mimetics and/or proteins.
27. The use of a protease, peptidase and/or hydrolase for the synthesis and/or N-terminal modification of peptides, peptide mimetics and proteins, said peptide, peptide mimetic and protein or N-terminally labeled species thereof being prepared by ligation of an amino component and a carboxyl component, and said carboxyl component having a leaving group.